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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/502,498	02/11/2000	Andrzej Kilian	191106.407C2	5251

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EXAMINER	
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ART UNIT	PAPER NUMBER
1652	

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22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/502,498	KILIAN ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on ~~May 15, 2002~~ Jan 21, 03.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,18,19 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,18,19 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: copies of the relevant pages of the US patent No. 6,166,178, copies of SEQ ID NO:46 and 45 of the instant application, and alignment of SEQ ID NO:46 with SEQ ID NO: 613 of the US patent 6,166,178.

The Amendment and Reply under 37 C.R.F. §1.111 filed on January 21 as paper 20 is acknowledged. Amendmnts to the claims have been entered as requested. New claims 65 and 66 are added. Claims 16, 18-22 and 65-66 are pending and are the subject of this Office Action.

Detailed Office Action

1. Rejections

1.2. 35 U.S.C. 112, second paragraph

Claims 18, 65 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18, from which claims 65 and 66 depend, is confusing. It appears to be intended to be broader than the claim 16 from which it depends, as it appears to intend to encompass non-naturally occurring variants of human telomerase splice variants as well as the naturally occurring variants as well. The recitation of "a variant thereof " in the third line of the claim is in accordance with the meaning of the term "variant" given on page 8, line 12:

> " Within the contest of this invention, it should be understood that telomerases of this invention include not only wild type- protein [SEQ ID NO:2, MW], but also variants (including alleles) of the wild-type protein sequence. Such variants may not necessarily exhibit enzymatic function. Briefly, such variants may result from

natural polymorphisms, including RNA splice variants, generated by genetic recombination, or be synthesized by recombinant methodology, and moreover, may differ from wild-type protein by one or more amino acid substitutions, insertions, rearengements or the like. Typically, when the result of synthesis, amino acid substitutions are conservative, i.e., substitution of amino acids within groups of polar, non-polar, aromatic, charged, etc. amino acids. In the region of homology to the wild-type sequence in the RTase motif regions variants will preferably have at least 90% amino acid sequence identity, and within certain embodiments, greater than 925, 95% or 97% identity. Outside the RTase motif regions variants will preferably have 75% amino acid identity, and within certain embodiments, at least 80%, 85%, 90%, 92%, 95% of 97% identity."

Therefore, the scope of claim 18 is broader than that of the base claim 16 that is limited to splice variants that are produced naturally.

1.2. 35 U.S.C. 112, first paragraph

Rejection of claim 18 for the error in residue No. 18 of SEQ ID NO: 46 are withdrawn because the applicants filed the corrected Sequence Listing.

Claim 16, and dependent claims 18-19, 22 and 65-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a large and variable genus of polypeptides for which the description of structure is insufficient in the claims and specification. The disclosure fails to sufficiently describe the genus of isolated proteins that comprise a splice variant of any human telomerase gene. The representative species disclosed by the specification are limited to splice variants of human telomerase gene of SEQ ID NO:1. This is insufficient to put someone skilled in the art in possession of the characteristic features of other species of the genus of proteins comprising a splice variant of any human telomerase gene. Neither the structure nor the function of all proteins comprising a splice variant of human telomerase are sufficiently described in the specification. The specification provides the amino acid structure and function encoded by many splice variants of SEQ ID NO:1, but not of any protein comprising them, nor of splice variants of other human telomerase. The genus of proteins comprising any splice variant of the human telomerase of SEQ ID NO:2 is a highly variable genus including proteins with telomerase activity, telomerase inhibitory activity, and other functions as well. As such, the disclosed species are insufficient to sufficiently describe the features of the claimed genus.

Changing the language of claim 16 from "comprising" to "consisting of" and specifying the gene of SEQ ID NO:1, i.e., "An isolated protein consisting of a splice variant of the human telomerase gene of SEQ ID NO:1" would obviate this rejection.

In their Remarks applicant write, "The Examiner Alleges that claim 19, which is directed to the fragment of the splice variant of human telomerase protein of claim 16, lacks the written description of a structure. However, the specification provides disclosure of 128 splice variants of human telomerase with different mRNA sequences (see page 22, lines 1-10 and Table 1 and Figure 11. This provides adequate written description for these splice variants and fragments of these variants" (page 2, line 15 of Amendment).

This argument of Applicants is found persuasive although the number of disclosed splice variant is lower. According to the Table 1 mentioned by Applcants, they disclosed 98 splice variants.

1.3. 35 USC section 102

Claim 16, 18, 19, 22, 65 and 66 are rejected under 35 U.S.C. 102(e) as being anticipated by Cech et al in the US Patent No. 6,166,178, issued December 26, 2000, with priority to Oct. 1996.

Claim 16 of the instant application is directed to an isolated protein comprising any splice variant of the human telomerase protein. Claim 19 and 65 are is directed to any fragment of splice variant of human telomerase. Claims 22and 66 are directed to any 10-100 amino acid long fragment of any splice variant of the human telomerase.

Applicants's arguments regarding the date of disclosure of so called delta 182 variants of Cech et al. are found persuasive. Thus rejection of claim 16 based on anticipation by delta 182 variant of Cech et al. is withdrawn. However, the claim remains rejected as directed to an isolated protein comprising a splice variant of human telomerase.

Claim 16 is rejected under 35 U.S.C. 102(e) as being anticipated by SEQ ID NO: 5 and 225 of the patents. Both sequences of the patent comprise splice variants of SEQ ID NO: 35. Sequence SEQ ID NO:5 comprises also SEQ ID NO:39 of the instant application; see the enclosed sequence alignements.

In respect to claim 19 and 22, Cech et al. teach human telomerase fragments (polypeptides) as one of the embodiments of their invention, (column 7, line 38 and further, also column 77, line 42). The fragments may be used as inhibitors of telomerase activity and as such used in pharmaceutical compositions. Cech et al teach, for example, motifs T, 1and 2, having the length of 10-100 amino acids, as may be seen from the enclosed Fig. 1 and 2 of the 6,166,178 patent.

Claim 18 is directed to a protein comprising a sequence that is at least 75% identical to SEQ ID NO: 46. SEQ ID NO: 613 of the US patent 6,166,178 comprises amino acid sequence that is in 98.7% identical to SEQ ID NO: 46. In addition SEQ ID NO: 225 of the US Patent 6,093.809 is in 99.6% identical to SEQ ID NO: 46 of the instant application. Thus SEQ ID NO: 613 of the US Patent 6,166,178 and SEQ ID NO: 225 of the US Patent 6,093.809 anticipate the claim; see the enclosed sequence search.

In their response to this rejection Applicants write "actually SEQ ID NO: 611 is the sequence contained in the Examiner's sequence search." According to the records, the sequence search print sent to Applicants contains alignment of SEQ ID NO:46 with SEQ ID NO: 613, page 5, right side, Result 5, through page 6. The print also contains SEQ ID NO:611 on the left side of page 5, without the description "Result 4", which is on page 4 that was not copied. Both sequences, SEQ ID NO:613 and 611, as well as SEQ ID NO:225, can be used in rejection.

Further Applicants argue, "Applicants submit that SEQ ID NO:611, is not a splice variant of human telomerase protein but rather is identified as a 'full length hTRT' in Cech in the text preceding the sequence."

The argument of Applicant has been fully considered but is not found persuasive. The 'full length hTRT' is not excluded by Aplicants from the disclosed genus of splice variants of the human telomerase, on contrary, it is included in Table 1 on page 22 as the splice variant of human telomerase comprising introns α and β (SEQ ID NO:25 and 27 in the instant application), but lacking introns Y, 1, 2 and 3 (SEQ ID NOs:18, 23, 29, and 30 in the instant application). The priority date for the disclosure of reference protein by Cech at al. is October 1, 1996.

In addition, Claim 18 is not directed to a splice variant of SEQ ID NO:46, but to a genus of protein comprising a splice variant, elected splice variant of SEQ ID NO:46, or a variant of SEQ ID NO:46, wherein said variant has at least 75% amino acid identity with SEQ ID NO:46." SEQ ID NO:613, which is 1189 amino acid long, comprises in positions 58-1189 a variant of splice variant of SEQ ID NO:46 that is in 98.9% identical

to SEQ ID NO:46. It is irrelevant whether SEQ ID NO:613 is identified as a "full length hTRT", "reference protein" or "wild type hTRT". In addition, SEQ ID NO:225, called "a reference protein" by Applicant, is a species of the genus of proteins comprising a variant of SEQ ID NO:46 that is at least 75% identical to SEQ ID NO:46, because the protein of SEQ ID NO:225 is 99.6% identical to SEQ ID NO:46.

New claims 65 and 66 are directed to any fragment of a protein comprising splice variant of human telomerase protein having amino acid sequence of SEQ ID NO: 46 or any fragment that is 10-100 amino acid long. The claims are rejected, for example, over the polypeptide fragment called motif T, having SEQ ID NO: 72 in the US Patent No. 6,166,178, and consisting of 46 amino acids. Motif T occupies residues 547-588 of SEQ ID NO: 46 of the instant application. Further rejections are possible over other motifs having SEQ ID NOs: 73 –79 in the US Patent No. 6,166,178.

In addition, claims 19 and 65 are rejected over amino acids disclosed by the Sigma Catalog, 1993. The claims are directed to any fragment of the human telomerase splice variants including amino acids and dipeptides.

The catalog discloses, for example, on page 59 the fragment of a human telomerase splice variant that is alanine (A7752).

Claims 19 and 65 are also rejected over dipeptide Gly-Gln that is disclosed in the same Sigma Catalog, on page 1089 (G5149). Dipeptide Gly-Gln occupies residues 252 and 253 of the splice variant identified by SEQ ID NO:46.

Claims 19, 22 and 65-55 would be allowable when limited to the novel fragments of splice variants identified by their sequence identification numbers.

The following is examiner's reasons for allowable subject matter. Applicants are the first who disclosed splice variants of human telomerase that are different than telomerase described in SEQ ID NO:2. The disclosure is of great importance for diagnosis and therapy of disorders related to carcinogenesis and aging.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Assistant Patent Examiner

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